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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,715	07/20/2006	Irit Sagi	29993	6189

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EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,715	SAGI ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35 and 42-57* is/are pending in the application.

4a) Of the above claim(s) *1-6, 15-34, 43-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-14 and 35-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/3/05, 6/6/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

With preliminary amendment of this application, the applicant, on date 12/14/2007 elected without traverse Group II (claims 7-14, 35, 42) for examination.

Election/Restriction

During preliminary amendment of this application, the applicant, on date 12/14/2007 elected Group II (claims 7-14, 35, 42), drawn to method of production of metalloprotein inhibitors wherein said metalloprotein is gelatinase B and said metal in MMP is zinc and using porphyrin as metal chelator for examination. Groups I and III-IV (claims 1-6, 15-34, 43-57) of election/restriction-office action of 11/14/07 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Priority

This application is a 371 of PCT /IL04/00308 filled 04/04/2004, which claims priority on US provisional applications of 60/460005 filled 04/04/2003.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 10/03/2005, and 06/06/2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the IDS statements.

Claim Objections

Claims 7-14, 35, 42 are objected for having non-elected subject matters.

Appropriate correction required.

Claim Rejections

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35 U.S.C 112 Rejection

35 U.S.C 112 1st Paragraph

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-14, 35, 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 7-14, 35, 42 are directed to a method of generating any metalloprotein inhibitor using a genus of antibodies wherein said antibodies generated by using any antigen composition comprising any metal ion bound to any chelating compound having structural and electronic properties similar to any metalloprotein functional domain and measuring inhibitory effect of the said antibody on any metalloprotein. Metalloprotein inhibitors

comprise many inhibitor types (antibody, chemical substance, etc). Claimed methods (directed to antibody type inhibitor) can not produce all these type of inhibitors. Furthermore, the claims are directed to use of antigen composition comprising a genus of metal ion bound chelating agent. Elicitation of immunogenicity and hence generation of antibody depends on the specific structure of the antigen (in this case type of metal and chelating agent). The specification teaches the a few method of producing metalloprotein inhibitor using antibodies arise to a few antigen comprising zinc and cobalt as metal and porphyrin as chelator. The specification does not disclose all the structure and function of all antigen composition comprising many metal ions and chelating agents that directed by these claims. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

In University of California v. Eli Lilly & Co., 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice,

reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Claim 7-14, 35, 42 are directed to a genus of any metalloprotein inhibitors using a genus of antibodies wherein said antibodies generated by using any antigen composition comprising any metal ion and any chelating agent. Elicitation of immunogenicity and hence generation of antibody depends on the specific structure of the antigen in this case type of metal and chelating agent. Moreover inhibitor produced by antibody generated by a hapten comprising one type of metal bound to one type of chelating agent will not probably inhibit different types metalloproteins. The specification teaches the structure of only a few metalloproteins and method of producing metalloprotein inhibitor using antibodies arise to comprising zinc and cobalt as metal and porphyrin as chelator. The specification does not disclose all the structure and function of all antigen composition comprising many metal ions and chelating agents that directed by these claims. Therefore one of skill in the art would not recognize from the disclosure that applicants' were in possession of the claimed

invention.

Applicants' are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Enablement

Claims 7-14, 35, 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of producing inhibitor using generating antibodies to Zn-metalloprotein, gelatinase B (MMP9) comprising a hapten comprising cobalt as metal and porphyrin as chelator (CoTCPP), does not reasonably provide enablement for any method of producing any metalloprotein inhibitor by using a genus of antibodies wherein said antibodies generated by using any antigen composition any metal ion conjugated to any chelator and measuring inhibitory effect of the said antibody on any metalloprotein. Antibody and method of generating said antibody to any hapten highly dependent on the structure of the hapten. Moreover inhibitor produce by antibody generated by a hapten comprising one type of metal bound to one type of chelating agent will not probably inhibit different types metalloproteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir.

1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claim(s).

Claims 7-14, 35, 42 are so broad as to encompass any method of producing any metalloprotein inhibitor by using a genus of antibodies wherein said antibodies generated by using any antigen composition any metal ion conjugated to any chelator. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of methods of producing metalloprotein inhibitor by using a genus of antibodies wherein said antibodies generated by using any antigen composition any metal ion conjugated to any chelator. Elicitation of immunogenicity and hence generation of catalytic antibody depends on the specific structure of the hapten in this case type of metal and nature and structure of chelating agents,. Moreover inhibitor produce by antibody generated by a hapten comprising one type of metal bound to one type of chelating agent will not probably inhibit different types metalloproteins. The specification neither describes all the structures of the metalloproteins nor structure of hapten comprising composition comprising said metal and metal bound chelating agent. Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of

experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claim(s).

The specification does not support the broad scope of the claims which encompass producing any metalloprotein inhibitor by using a genus of antibodies wherein said antibodies generated by using any antigen composition any metal ion conjugated to any chelator because the specification does not establish: (A) regions of the metal bound chelate structure that mimic functional domain of the metalloprotein and the structure of the said functional domain of the metalloprotein may be modified or arranged without effecting immune activity; (B) the general tolerance of immune activity to modification of the constituents of the conjugates and extent of such tolerance; (C) a rational and predictable scheme for modifying any chelating agent for immune activity with an expectation of obtaining the desired biological function and; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use all antibodies wherein said antibodies generated by using any antigen composition any metal ion conjugated to any chelator to produce metalloprotein inhibitors. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without

sufficient guidance, determination metal bound chelate structure that mimic functional domain of the metalloprotein and use it to produce antibodies and then use said antibodies to produce mtalloprotein inhibitor of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

CLAIM Rejection - 35 U.S.C 103a

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-14, 35, 42 are rejected under 35 U.S.C. 103(a) as obvious over Harada et al (Photochem. Photobio. 1999, pp298-302 from IDS) in view of Galvez et al. (JBC 2001, 276, pp 37491-37500, from IDS)) and Kleifeld et al. (JBC 2001, 276, pp 17125-17131, from IDS).

Galvez et al. teach monoclonal antibody, anti-MTI MMP mAbs, as metalloprotein inhibitor (whole article, especially page 37499, last paragraph and also a discussion of this article in applicant specification at page 4). However Harada et al. do not teach method of generating metalloprotein inhibitor using antibodies wherein said antibodies generated by using antigen composition comprising metal ion bound

to chelating compound having structural and electronic properties similar to metalloprotein functional domain. Kleifeld et al teach method of making metalloprotein inhibitor using the knowledge of structural and electronic properties similar to metalloprotein functional domain of metalloprotein (a discussion of this article in applicant specification at pages 3-4).

Harada et al. teach monoclonal antibody to Zn- TCPP type hapten and method of producing the said antibody. Zn- TCPP (a moiety having structural and electronic properties similar to metalloprotein functional domain) type hapten is similar antigen composition that applicant use in their method step, i.e., comprising metal ion (Co or Zn bound to chelating compound (TCPP) having structural and electronic properties similar to metalloprotein functional domain.

Therefore one knowledgeable in prior art is **motivated** by the knowledge taught by Kleifeld et al. and then use the method of production of monoclonal antibody as taught by Harada et al. and use said generated antibody to the method of producing metalloprotein inhibitor as taught by Galvez et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Mohammad Meah/
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